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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/822,975	04/12/2004	David A. Griffith	PC25409A	5681

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PFIZER INC.
PATENT DEPARTMENT, MS8260-1611
EASTERN POINT ROAD
GROTON, CT 06340

EXAMINER	
MOORE, SUSANNA	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 09/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/822,975	GRIFFITH ET AL.	
	Examiner	Art Unit	
	Susanna Moore	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17(part), 18, 19-24(part), 25, 26-32(part), 33, 34-39(part), 40, 41-46(part), 47, 48-53(part) and 54-123.* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/29,8/6,4/11,6/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-17(part), 18, 19-24(part), 25, 26-32(part), 33, 34-39(part), 40, 41-46(part), 47, 48-53(part) and 54-123.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 1-17(part), 19-24(part), 26-32(part), 34-39(part), 41-46(part), 48-53(part) and 123(part).

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-17(part), 18, 19-24(part), 25, 26-32(part), 33, 34-39(part), 40, 41-46(part), 47, 48-53(part) and 54-123, drawn to compounds of formula (I), wherein A= nitrogen, pyrazolopyridines, compositions and method of treatments thereof, classified in class 544, subclass 262, 230, 106 and class 514, subclass 262.1 and 234.2.

II. Claims 1-17(part), 19-24(part), 26-32(part), 34-39(part), 41-46(part) and 48-53(part), drawn to compounds of formula (I), wherein A= carbon, pyrazolopyrimidines, compositions and method of treatments thereof, classified in class 546, subclass 119 and 15, class 544, subclass 106 and class 514, subclass 303, 278 and 234.2.

III. Claim 123(part), drawn to a compound of formula (2e), 1H-pyrazoles, classified in class 548, subclass 364.1 and 271.4.

Groups I-III are independent and distinct from each other as they are drawn to compounds with divergent ring systems. Group (I) encompasses bicyclic compounds of formula (I) of claim 1, wherein A= nitrogen, pyrazolopyridines. Group (II) is drawn to bicyclic compounds, wherein A= carbon, pyrazolopyrimidines. The compounds of group (III) covers compounds represented by formula (2e) in claim 123, non-fused 1H-pyrazoles.

Each of groups I-III are directed to compounds which are recognized in the art as being distinct from one another because of their diverse chemical structure, their different chemical properties, modes of actions, different effects, and reactive conditions. It is noted that a reference disclosing a compound of one group would not necessarily disclose a compound of the other two groups. Additionally, the level of skill in the art is not such that one invention would be obvious over the other, i.e. they are patentable over each other. Chemical structures that are similar are presumed to function similarly, while chemical structures that are not similar are not presumed to function similarly. The presumption even for similar chemical structures though is not irrefutable, but may be overcome by scientific reasoning or evidence showing that the structure of the prior art would not have been expected to function as the structure of the claimed invention. Thus, by virtue of the different structures presented in groups I-III, these inventions are distinct. Note that in accordance with the holding of ***Application of Papesch, 50 CCPA 1084, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)***, and ***In re Lalu, 223 USPQ 1257 (Fed. Cir. 1984)***, chemical structures are patentably distinct where structures are either not structurally similar, or the prior art fails to suggest a function of a claimed compound would have been expected from a similar structure.

During a telephone conversation with Arlene Musser on September 7, 2006 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-17(part), 18, 19-24(part), 25, 26-32(part), 33, 34-39(part), 40, 41-46(part), 47, 48-53(part) and 54-123. Affirmation of this election must be made by applicant in replying to this Office action. Claims

1-17(part), 19-24(part), 26-32(part), 34-39(part), 41-46(part), 48-53(part) and 123(part) are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Pyrazolo[4,3-d]pyrimidine as CANNABINOID RECEPTOR LIGANDS AND USES THEREOF.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 99-122 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear what diseases and treatments Applicant is intending to encompass. Determining whether a given disease responds or does not respond to such a receptor antagonist and thus, covered by the claim language, will require extensive and potentially inconclusive clinical research. There is no standard list. Without such clinical research to identify the patients and diseases Applicants intend to treat, someone skilled in the art could not determine the metes and bounds of the claim. Hence, the claims are indefinite. The passage in the Specification spanning pages 48-49 gives an impressively long list of such diseases. However, that passage uses the open term "includes." What other diseases, in addition to those listed, are being claimed? The Examiner suggests listing the specific diseases, which Applicant intends to treat being mindful of the enablement rejection made below.

Claims 99-123 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The specification does not set forth any steps involved in determining how to identify "an animal in need of such treatment." It is unclear what diseases and treatments applicant is intending to encompass. The Specification on pages 48-49 lists an impressive amount of vastly different diseases. However, it uses open language. Is this the entire scope of the therapeutic claims or are there other diseases? Does everyone need such inhibition, i.e. does

claim 99 cover treating healthy people?

Claims 98, 103, 109, 115 and 120 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The terms "analog" or "analog thereof" are indefinite. What are these analogs of leptin and dehydroepiandrosterone?

Claims 1, 2, 4-6, 11, 19, 21, 34-36, 55, 57, 58-60, 63, 69, 71, 80 and 82 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "acyl" is vague. The reason is that there are multiple definitions, and there is no one, generally accepted, definition. The broadest notion sets no limitation at all on the nature of the acid used to form the acyl. Thus, the Wikipedia entry says "the term acyl or acyl group refers to a functional group obtained from an acid by removal of a hydroxyl group." If you take OH from nitric acid, you have nitro group, so nitro is an acyl. If you take OH off of hypochlorous acid (Cl-OH), you get Cl as acyl. Hydrogen peroxide is a (very) weak acid, so take away OH, and you have OH left as an acyl. What does Applicant intend? Please be sure Applicant's response coincides with the Specification.

Claims 107-110 and 118-122 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "pharmaceutical agent" is vague. Agent for what?

What are these pharmaceutical agents? Are these preservatives? Maybe surfactants? What does Applicant intend? Is this supposed to cover all drugs?

Claims 99-122 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Such a utility cannot be deemed enabled.

Pursuant to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(A) Breadth of claims.

(a) Scope of the compounds. The instant claim embraces millions of compounds with a pyrazolo[4,3-d]pyrimidine framework with a variation of substituents at four different positions. These variations to the scaffold give a diverse range of compounds, which provide different

physical and chemical properties to the compounds of formula (I).

(b) Scope of the diseases covered. Claims 99-122 are drawn to a method of treating (I) weight loss, (II) obesity, (III) bulimia, (IV) depression, (V) atypical depression, (VI) bipolar disorders, (VII) psychoses, (VIII) schizophrenia, (IX) behavioral addictions, (X) suppression of reward related behaviors, (X) alcoholism, (XI) tobacco abuse, (XII) dementia, (XIII) seizure disorders, (XIV) epilepsy, (XV) attention deficit disorders, (XVI) Parkinson's disease, (XVII) inflammation, (XVIII) gastrointestinal disorders and (XX) type II diabetes. The scope also covers a condition or disorder which is modulated by a cannobinoid receptor antagonist, for which there is no standard list. The scope of some of the "umbrella" terms will be discussed below.

(II) Bulimia nervosa, more commonly known as bulimia, is an eating disorder. It is a psychological condition in which the subject engages in recurrent binge eating followed by an intentional purging. This purging is done in order to compensate for the excessive intake of the food and to prevent weight gain.

(III) Obesity, a condition which is just the opposite of bulimia nervousa. Obesity is a condition in which the natural energy reserve, stored in the fatty tissue of humans and mammals is increased to a point where it is thought to be a significant risk factor in certain health conditions, leading to increased mortality. Obesity is a disease characterized by being overweight. There are many factors that can cause obesity, including genetics, stress, and hypothyroidism just to name a few.

(XII) Dementia is the progressive decline in cognitive function due to damage or disease in the brain beyond what might be expected from normal aging. Dementia is a non-specific term

that encompasses many disease processes, just as fever is attributable to many etiologies, e.g. Alzheimer's disease, vascular dementia (including Binswanger's disease), dementia with Lewy bodies, frontotemporal lobar degeneration (FTLD, including Pick's disease), frontotemporal dementia, semantic dementia, progressive non-fluent aphasia, Creutzfeldt-Jakob disease, Huntington's disease, Parkinson's disease, HIV infection, head trauma, hypothyroidism, vitamin B1 (thiamine) deficiency, Vitamin B12 deficiency, Vitamin A deficiency, depressive pseudodementia, normal pressure hydrocephalus and tumors.

(XVI) Parkinsons disease is a degenerative disorder of the central nervous system which is characterized by muscle rigidity, tremor, a slowing of physical movement (bradykinesia), and in extreme cases, a loss of physical movement (akinesia). The primary symptoms are the results of excessive muscle contraction, normally caused by the insufficient formation and action of dopamine, which is produced in the dopaminergic neurons of the brain.

(XVII) An inflammatory disease can be defined as a disease characterized by inflammation anywhere in the body. Inflammation is the body's first response to injury, e.g. trauma, infection irritation, etc. This is a non-specific immune response. Some examples of inflammatory diseases are as followed, but not limited to: allergies, appendicitis, arteritis, arthritis, asthma, blepharitis, bronchiolitis, bronchitis, bursitis, cervicitis, cholangitis, cholecystitis, chorioamnionitis, colitis, conjunctivitis, cystitis, dacryoadenitis, dermatitis, dermatomyositis, encephalitis, endocarditis, endometritis, enteritis, enterocolitis, epicondylitis, epididymitis, fasciitis, fibrositis, gastritis, gastroenteritis, gingivitis, hepatitis, hidradentitis supparativa, ileitis, immune reconstitution inflammatory syndrome (IRIS), laryngitis, mastitis, meningitis, myelitis, myocarditis, myositis, nephritis, omphalitis, oophoritis, orchitis, osteitis,

otitis, pancreatitis, parotitis, pelvic inflammatory disease (PID), pericarditis, peritonitis, pharynx, pleuritis, phlebitis, pneumonitis, protitis, prostatitis, rhinitis, salpingitis, sinusitis, stomatitis, synovitis, tendonitis, tonsillitis, uveitis, vaginitis, vasculitis and vulvitis.

(XVIII) Gastrointestinal disorders can be defined as any disease or disorder associated with the GI tract, which include the mouth, esophagus, stomach, intestines, rectum and anus. Other organs, such as the spleen, bile ducts, gall bladder, liver and pancreas, can also be a cause of gastrointestinal disorders. As recited, the scope of the claim can include, but is not limited to, tooth decay, periodontal disease, abscesses, canker sores, cold sores, oral cancer, gastroesophageal reflux disease, dysphagia, esophagus cancer, circopharyngeal incoordination, achalasia, diverticula, burning mouth syndrome, pancreas cancer, Crohn's disease, colon polyps, diverticular disease, intestinal parasites, salivary gland disease, sialhorria, dentigerous cyst, glossitis, benign migratory, Ludwig's Angina, Melkerson-Rosenthal Syndrome, xerostamia, Pierre-Robin Syndrome, diabetes, lactose intolerance, bruxism,ulcerative colitis, cystic fibrosis, pernicious anemia, tropical sprue, cirrhosis, Bassen-Kornzweig syndrome, pancreatitis, Shwachman-Diamond syndrome, anal cancer, acute pancreatitis, anal fissure, anal fistula, colorectal cancer, hemorrhoids, perirectal abscess, proctitis, rectal prolapse, functional constipation, liver cancer, diarrhea, ankyloglossia, Irritable Bowel Syndrome, functional dyspepsia, peptic ulcer, intussusception, Coeliac disease, Whipple's disease, lymphoma, incontinence, chronic pancreatitis, Hirschsprung's disease, infant regurgitation, biliary disorder, hemochromatosis, Wilson disease, tyrosinemia, alpha 1 antitrypsin defiency, glycogen storage disease, primary sclerosing cholangitis, hepatitis A, hepatitis B, hepatitis C, Reyes's syndrome.

These are just some of the diseases embraced by the scope of claims 99-122.

(B) The nature of the invention and predictability in the art: The invention is directed toward medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(C) Direction or Guidance: That provided is very limited. The dosage range information, found on page 49 of the Specification gives 0.7-7,000 mg/kg, which is very broad. Moreover, this is generic, the same for the many disorders covered by the Specification. Thus, there is no specific direction or guidance regarding a regimen or dosage effective specifically for any and all diseases encompassed by the scope of claims 99-122.

(D) State of the Prior Art: These compounds are substituted pyrazolo[4,3-d]pyrimidine with a substitution pattern at four positions. So far as the examiner is aware, no substituted pyrazolo[4,3-d]pyrimidine of any kind have been used for the treatment of any and all the diseases encompassed by the scope of claims 99-122.

(E) Working Examples: The invention is drawn to the therapy of all the diseases listed under the Scope of diseases. There are several prophetic in vitro assays, including inhibition assays of human and rat CB1 and CB2 assays and activation assays, including GTPγ assay, FLIPR-based assay, and c-AMP assay. There are several prophetic in vivo assays drawn to locomotor activity,

catalepsy, hypothermia, hot plate, food intake, alcohol intake and oxygen consumption. There are no working examples or data in the Specification drawn to this utility to support the use of substituted pyrazolo[4,3-d]pyrimidine to treat any or all the diseases covered by the Scope of diseases.

(F) Skill of those in the art: These diseases and disorders cannot be treated generally by any one drug. These are all different diseases and disorders, which occur at different locations and by different modes of action in the body. Hirschsprung's disease, one of the many mentioned above, is a disorder, which is primarily treated with surgery. The instant compounds, substituted pyrazolo[4,3-d]pyrimidine, are recited as useful in treating any or all functional gastrointestinal disorders, for which applicants provide no competent evidence. Coeliac disease is untreatable. Hepatitis is treatable with antiviral agents, a property these compounds not disclosed to have.

Obesity, a condition which is just the opposite of bulimia nervousa, is not treated with the same pharmacotherapy as bulimia nervousa. They are at opposite ends of eating disorders.

The different inflammations are not treated equally, i.e. PID is treated with antibiotics while an appendicitis is treated with the removal of the appendix (surgery).

To date, there are no CB1 antagonists used to treat Parkinson's disease patients or dyskinesias. Note that Parkinson's disease itself is not treatable, current therapies are directed only to symptom alleviation.

Note that many of the diseases listed in the Scope of diseases are "umbrella" terms that are very broad in scope. Such as dementia, which involves more than memory disorders, and that

most memory disorders are not a form of dementia.

(G) The quantity of experimentation needed: Owing especially to the factors of A, C, E and F, the amount of experimentation is expected to be high.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Claims 1-123 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for other forms, does not reasonably provide enablement for solvates or hydrates. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claims 1-123 are drawn to solvates or hydrates. But the numerous examples presented all failed to produce a solvate or hydrate. These cannot be simply willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there is no evidence that such compounds

exist... the examples of the '881 patent do not produce the postulated compounds... there is ... no evidence that such compounds even exist." The same circumstance appears to be true here: there is no evidence that solvates or hydrates of these compounds actually exist; if they did, they would have formed. No specific solvates or hydrates are mentioned and no direction for making any solvate or hydrate is disclosed. Hence, applicants must show that solvates can be made, or limit the claims accordingly.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susanna Moore whose telephone number is (571) 272-9046. The examiner can normally be reached on M-F 8:00-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SM

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